

LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of the claims in the application.

1. (Amended) An artificial low-density lipoprotein (LDL) ~~LDL~~ particle comprising an outer phospholipid monolayer and a solid lipid core, wherein the outer phospholipid monolayer comprises at least one recombinant apolipoprotein and the solid lipid core contains at least one therapeutic agent.
2. (Original) The artificial LDL particle of claim 2, wherein the at least one apolipoprotein is ApoE.
3. (Original) The artificial LDL particle of claim 2, wherein the at least one apolipoprotein is ApoE3.
4. (Original) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is selected from the group consisting of: amino acids, peptides, proteins, carbohydrates and lipids.
5. (Original) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is a conjugate formed between cholesterol and an agent selected from the group consisting of: amino acids, peptides, proteins, carbohydrates and lipids.
6. (Original) The artificial LDL particle of claim 1, wherein the outer phospholipid monolayer comprises phosphatidylcholine and at least one apolipoprotein.
7. (Original) The artificial LDL particle of claim 6, wherein the at least one apolipoprotein is ApoE.
8. (Original) The artificial LDL particle of claim 1, wherein the particle has a diameter between about 15 and 50 nm.
9. (Original) The artificial LDL particle of claim 1, wherein the particle has a diameter between about 20 and 30 nm.

10. (Original) The artificial LDL particle of claim 1, wherein the particle has a density between about 1.00 and 1.07 g/ml.
11. (Original) The artificial LDL particle of claim 1, wherein the particle has a density between about 1.02 and 1.06 g/ml.
12. (Original) The artificial LDL particle of claim 1, wherein the particle has a serum stability of at least two hours.
13. (Original) The artificial LDL particle of claim 1, wherein the particle is transported across the blood-brain barrier (BBB) by transcytosis.
14. (Original) The artificial LDL particle of claim 1, wherein the particle has at least a 3-fold greater uptake specificity for brain compared to liver.
15. (Original) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is a conjugate formed between cholesterol and adriamycin.
16. (Original) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is a conjugate formed between cholesterol and tetracycline.
17. (Original) The artificial LDL particle of claim 15, wherein the cholesterol and adriamycin of the conjugate are linked by an ester bond.
18. (Original) The artificial LDL particle of claim 16, wherein the cholesterol and tetracycline of the conjugate are linked by an ester bond.
19. (Amended) An artificial low-density lipoprotein (LDL) ~~LDL~~ particle for delivery of an agent across the blood-brain barrier comprising an outer phosphatidylcholine monolayer, a solid lipid core comprising fatty acyl-cholesterol esters, and ApoE in the outer monolayer.
20. (Original) The artificial LDL particle of claim 19, wherein the solid lipid core further comprises cholesterol.

21. (Original) The artificial LDL particle of claim 19, wherein the ApoE in the outer monolayer is ApoE3.
22. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 1 and a pharmaceutically acceptable carrier.
23. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 4 and a pharmaceutically acceptable carrier.
24. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 5 and a pharmaceutically acceptable carrier.
25. (Amended) A conjugate comprising cholesterol linked to adriamycin or tetracycline, a therapeutic agent selected from the group consisting of: ~~amino acids, peptides, proteins, carbohydrates and lipids.~~
26. (Amended) The conjugate of claim 25, wherein the cholesterol is linked to adriamycin or tetracycline through an ester linkage, therapeutic agent is selected from the group consisting of: ~~neurotrophic factors, growth factors, enzymes, neurotransmitters, neuromodulators, antibiotics, antiviral agents, antifungal agents and chemotherapeutic agents.~~
27. (Amended) The conjugate of claim 26, 25, wherein the cholesterol therapeutic agent is linked to adriamycin through an ester linkage.
28. (Amended) The conjugate of claim 27, wherein the conjugate has the structure in Figure 5, ~~adriamycin and cholesterol are linked by an ester linkage.~~
29. (Amended) The conjugate of claim 26-25, wherein the cholesterol therapeutic agent is linked to tetracycline through an ester linkage.

30. The conjugate of claim 29, wherein the conjugate has the structure in Figure 6, ~~tetraacycline and cholesterol are linked by an ester linkage.~~
31. (Original) The artificial LDL particle of claim 4, wherein the therapeutic agent is selected from the group consisting of: neurotrophic factors, growth factors, enzymes, neurotransmitters, neuromodulators, antibiotics, antiviral agents, antifungal agents and chemotherapeutic agents.
32. (Original) The artificial LDL particle of claim 5, wherein the therapeutic agent is selected from the group consisting of: neurotrophic factors, growth factors, enzymes, neurotransmitters, neuromodulators, antibiotics, antiviral agents, antifungal agents and chemotherapeutic agents.
33. (Original) The artificial LDL particle of claim 1, wherein the outer phospholipid monolayer further comprises one or more oxysterols and/or an additional apolipoprotein selected from the group consisting of ApoB and ApoE4.
34. (Amended) A method of producing an artificial low-density lipoprotein (LDL) ~~LDL~~ particle of claim 1 comprising the steps of: 1) suspending phospholipids containing conjugated or unconjugated therapeutic agent in a buffer solution; 2) sonicating the solution to form the outer phospholipid monolayer and solid lipid core; and 3) adding a solution comprising at least one apolipoprotein, wherein the at least one apolipoprotein is ApoE and is incorporated into the outer phospholipid monolayer.
35. (Original) The method of claim 34, wherein the artificial LDL particles produced have a diameter between 10 and 50 nm.
36. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 22 to a mammal in need thereof.
37. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 23 to a mammal in need thereof.

38. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 24 to a mammal in need thereof.
39. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 22 and instructions for use.
40. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 23 and instructions for use.
41. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 24 and instructions for use.